REMARKS

Claims 1-24 were pending in the subject application. Applicants have canceled claims 21, 22 and 24 amended claims 1-20 and 23 and added new claims 25-30.

In the March 23, 2001 Office Action, the Examiner set forth rejections of the claims and objection to the specification under 35 U.S.C. § 112.

In response, applicants have amended the specification and claims to clarify any ambiguities the Examiner referred to.

Specifically, applicants point out that there are three distinct terms being used in the subject application, the terms being:

-pharmaceutically acceptable component;

-pharmacologically active agent; and

-pharmaceutically acceptable carrier.

As used in the subject application, a "pharmaceutically acceptable component" may be a "pharmacologically active agent", which is described, for example on page 5, line 19 to page 8, line 9 of the subject specification, as amended.

However, a "pharmaceutically acceptable carrier" is yet another component which may be present in the claimed composition, which is defined on page 8, line 11 to page 9, line 13 of the specification, as amended.

In view of the foregoing amendments to the specification and claims, applicants respectfully request reconsideration and withdrawal of the rejections and objections set forth in the March 23, 2001 Office Action.

If any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

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09.20.01
Date

ATTACHMENT A

SPECIFICATION AS AMENDED TO SHOW CHANGES

On page 5, lines 4-11

The present invention surprisingly overcomes the problems referred to hereinbefore, which hinder topical drug absorption, by providing a topical composition comprising a eutectic mixture of at least two pharmaceutically acceptable components which are both pharmacologically active agents in their lipophilic (substantially water-insoluble) form, the eutectic mixture being dispersed in, but not substantially dissolved in, a hydrophilic, pharmaceutically acceptable carrier.

On page 5, lines 13-23

Accordingly, the invention provides a topical composition comprising an emulsion of at least one discontinuous phase in a continuous phase, the or each discontinuous phase including a eutectic mixture of first and second pharmaceutically acceptable components which are both pharmacologically active agents and the continuous phase being provided by a pharmaceutically acceptable carrier, the eutectic mixture having a melting point below 40°C. Preferably, the first pharmacologically active agent has a melting point between 35 and 75°C, preferably 40-50°C, and the second pharmacologically active agent has a melting point between -40 and 150°C, preferably between -5 and 90°C.

Page 8, lines 4-9

~~As used herein, the term pharmacologically acceptable component' means any~~ The pharmaceutically acceptable component may also be an agent not intended for use in the prophylaxis or therapy of any condition affecting the health of the human or animal species and includes, but is not limited to, lauric acid, stearyl alcohol, menthol, thymol, cinnamic acid or an ester thereof.

Page 8, lines 11-24

~~Said~~ The pharmaceutically acceptable carrier according to this invention should be suitable for administration of the eutectic mixture; should not adversely interfere with the formation and stability of said mixture; and should be suitable for topical application. Suitable topical compositions include gels, lotions, suspensions, creams, aerosol sprays, transdermal patches, medicated dressings and soft gelatin capsules for rapid gastrointestinal absorption. Preferably, the pharmaceutical carrier of use in the invention should be substantially hydrophilic, said carrier containing substantially, preferably essentially, water as the continuous phase and there should be no lipophilic phase present, other than that formed by the eutectic mixture of the composition of the invention.

ATTACHMENT B

CLAIMS AS AMENDED WITH MARKINGS TO SHOW CHANGES

SERIAL NO. 09/423,715

--1. (Amended) A topical composition for mutual enhancement of transdermal permeation of at least first and second pharmaceutically acceptable components which are both pharmacologically active agents, the composition comprising an emulsion of at least one discontinuous phase in a continuous phase, the or each discontinuous phase [including] comprising a eutectic mixture of first and second pharmacologically active agents and the continuous phase [being provided by] comprising a pharmaceutically acceptable carrier, the eutectic mixture having a melting point below 40°C; and at least one compatible emulsifying agent, with the proviso that the at least first and second pharmacologically active agents are each not local anaesthetics.

--2. (Amended) [A] The topical composition according to Claim 1, in which the first pharmacologically active agent has a melting point between 35 and 75°C, [preferably 40-50°C] and the second pharmacologically active agent has a melting point between -40°C and 150°C [, preferably between -5 and 90°C].

--3. (Amended) [A] The topical composition according to Claim 1 [or 2], in which the topical composition additionally includes, in the eutectic mixture, a third pharmaceutically acceptable component.

--4. (Amended) [A] The topical composition according to Claim 3, in which the third pharmaceutically acceptable component

has a melting point between 40 and 150°C [, preferably between 40 and 75°C].

--5. (Amended) [A] The topical composition according to Claim 3 or 4, in which the third component is a third pharmacologically active agent.

--6. (Amended) [A] The topical composition according to [any one of Claims 3-5] Claim 1, in which the topical composition additionally includes, in the eutectic mixture, a fourth pharmaceutically acceptable component.

--7. (Amended) [A] The topical composition according to Claim 6, in which the fourth pharmaceutically acceptable component has a melting point between 40 and 150°C [, preferably between 40 and 75°C].

--8. (Amended) [A] The topical composition according to Claim 6 or 7, in which the fourth component comprises a fourth pharmacologically active agent.

--9. (Amended) [A] The topical composition according to [any one of the preceding claims] Claim 1, in which said at least one discontinuous phase contains no co-solvent or additional oil phase, so that the eutectic mixture substantially [, preferably essentially,] comprises the or each discontinuous phase of the emulsion.

--10. (Amended) [A] The topical composition according to [any one of the preceding claims] Claim 1, in which the first pharmacologically active agent is selected from the group consisting of triclosan, chlorocresol, chlorbutanol, methyl nicotinate, triprolidine, promethazine, trimeprazine,

sulfiram, oxybutynin, capsaicin, testosterone enanthate [or] and choline salicylate.

--11. (Amended) [A] The topical composition according to [any one of the preceding claims] Claim 1, in which the second pharmacologically active agent is selected from the group consisting of ~~triclosan, chloroceresol, capsaicin, trimeprazine, choline salicylate, methyl nicotinate;~~ non-steroid anti-inflammatory ~~agents selected from~~ arylpropionic acid derivatives ~~such as ibuprofen, ketoprofen, fenoprofen and flurbiprofen~~, aryl acetic acid derivatives, ~~such as etodolac; and~~ arylcarboxylic acids~~;~~, narcotic analgesics ~~such as fentanyl;~~, anti-fungal agents ~~such as econazole and ketoconazole;~~, antibacterial agents ~~such as mupirocin, chlorbutanol, clindamycin and iodine;~~, anticholinergics ~~such as oxybutynin;~~, anthelmintics ~~such as tetramisole;~~, antihistaminics ~~such as triprolidine and promethazine;~~, and antihypertensives ~~such as propranolol~~.

--12. (Amended) [A] The topical composition according to Claim [5 or] 8, in which the third and fourth pharmacologically active agents are each selected from the group consisting of ~~triclosan; chloroceresol; capsaicin, trimeprazine, choline salicylate, methyl nicotinate;~~ non-steroid anti-inflammatory ~~agents selected from~~ arylpropionic acid derivatives ~~such as ibuprofen, ketoprofen, fenoprofen and flurbiprofen;~~ , aryl acetic acid derivatives ~~such as etodolac; and~~ , ~~arylcarboxylic acids;~~ , narcotic analgesics ~~such as fentanyl;~~ , anti-fungal agents, ~~such as econazole and ketoconazole;~~ antibacterial agents, ~~such as mupirocin,~~

~~chlorbutanol, clindamycin and iodine;~~ anticholinergics, ~~such as oxybutynin;~~ antihypertensives, ~~such as propranolol;~~ antihistaminics, ~~such as triprolidine and promethazine;~~ and anthelmintics ~~such as tetramisole~~.

--13. (Amended) [A] The topical composition according to Claim 3 or 4, in which the third [component is a] pharmaceutically acceptable component is selected from lauric acid, stearyl alcohol, menthol, thymol, cinnamic acid or an ester thereof.

--14. (Amended) [A] The topical composition according to [any one of the preceding claims] Claim 1, in which the pharmaceutically acceptable carrier is substantially hydrophilic, said carrier containing substantially [, preferably essentially,] water as the continuous phase.

--15. (Amended) [A] The topical composition according to [any one of the preceding claims] Claim 1, in which the pharmaceutically acceptable carrier contains at least one gelling or suspension agent.

--16. (Amended) [A] The topical composition according to Claim 15, in which the gelling or suspension agent is selected from the group consisting of carbomers, modified cellulose derivatives, naturally-occurring synthetic or semi-synthetic gums ~~such as xanthan gum, acacia and tragacanth~~, modified starches, co-polymers ~~such as those formed between maleic anhydride and methyl vinyl ether~~, colloidal silica and methacrylate derivatives or a mixture thereof.

--17. (Amended) [A] The topical composition according to [any one of the preceding claims] Claim 1, in which the topical composition is in the form of a gel, lotion, suspension, cream, aerosol spray, transdermal patch, medicated dressing or soft gelatin capsule.

--18. (Amended) [A] The topical composition according to [any one of the preceding claims] Claim 1, in which the emulsifying agent is selected from the group consisting of non-ionic, cationic and anionic surfactants.

--19. (Amended) [A] The topical composition according to Claim 18, in which the emulsifying agent is a non-ionic surfactant.

--20. (Amended) [A] The topical composition according to [any one of the preceding claims] Claim 1, in which the at least two pharmacologically active agents are structurally and/or pharmacologically diverse.

--23. (Amended) A method for mutual enhancement of dermal permeation of at least first and second pharmaceutically acceptable components which are both pharmacologically active agents, the method comprising applying a topical composition for mutual enhancement of transdermal permeation of at least first and second pharmacologically active agents, the composition comprising an emulsion of at least one discontinuous phase in a continuous phase, the or each discontinuous phase [including] comprising a eutectic mixture of first and second pharmacologically active agents and

the continuous phase [being provided by] comprising a pharmaceutically acceptable carrier, the eutectic mixture having a melting point below 40°C; and at least one compatible emulsifying agent, with the proviso that the at least first and second pharmacologically active agents are each not local anaesthetics, to an accessible body surface of an animal.

Please add new claims 25-30 as follows:

--25. (New) The topical composition according to claim 2, wherein the first pharmacologically active agent has a melting point between 40 and 50°C, and the second pharmacologically active agent has a melting point between -5 and 90°C.

--26. (New) The topical composition according to claim 4, wherein the third pharmaceutically acceptable component has a melting point between 40 and 75°C.

--27. (New) The topical composition according to claim 7, wherein the fourth pharmaceutically acceptable component has a melting point between 40 and 75°C.

--28. (New) The topical composition according to claim 11, wherein the second pharmacologically active agent is selected from the group consisting of triclosan, chlorocresol, capsaicin, trimeprazine, choline salicylate, methyl nicotinate, ibuprofen, ketoprofen, fenoprofen, flurbiprofen, etodolac, fentanyl, econazole, ketoconazole, mupirocin, chlorbutanol, clindamycin, iodine, oxybutynin, tetramisole,

triprolidine, promethazine, and propranolol.

--29. (New) The topical composition according to Claim 12, wherein the third and fourth pharmacologically active agents are each selected from the group consisting of triclosan, chlorocresol, capsaicin, trimeprazine, choline salicylate, methyl nicotinate, ibuprofen, ketoprofen, fenoprofen, flurbiprofen, etodolac, arylcarboxylic acids, fentanyl, econazole, ketoconazole, mupirocin, chlorbutanol, clindamycin, iodine, oxybutynin, propranolol, triprolidine, promethazine, and tetramisole.

--30. (New) The topical composition according to Claim 16, wherein the gelling or suspension agent is selected from the group consisting of xanthan gum, acacia, tragacanth, maleic anhydride copolymers, methyl vinyl ether, and a mixture thereof.